

Keratoconus- Treatment options

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Introduction

Keratoconus is a bilateral noninflammatory corneal ectasia with an incidence of approximately 1 per 2,000 in the general population.^{1, 2, 3} It has well described clinical signs, but early forms of the disease may go undetected unless the corneal topography is studied. Classic histopathologic features include stromal thinning, iron deposition in the epithelial basement membrane, and breaks in Bowman's layer. Keratoconus is most commonly an isolated disorder although an association with Down syndrome, Leber's congenital amaurosis, and mitral valve prolapsed has been described. The differential diagnosis of keratoconus includes keratoglobus, pellucid marginal degeneration and Terrien's marginal degeneration. Typically, the patients present in early adulthood and visual symptoms result from irregular astigmatism and increasing myopia^{4, 5}. It is reported to have bilateral involvement in over 90% of patients, with asymmetric presentation. Most keratoconus patients can be adequately corrected with spectacles or contact lenses. However,

in recent years there has been a rapid advancement in the therapeutic options for keratoconus management.

Spectacle Correction

In the early stages of keratoconus, the patient's refractive error can often be successfully managed with spectacle lenses. It is important to communicate to the patient that there is no evidence to support the theory that early contact lens intervention is of therapeutic benefit in preventing or lessening the progression of the disease. However, wearing contact lenses typically provides the patient with better visual acuity than can be obtained with glasses by neutralizing the regular and irregular refractive errors induced by the condition.

Contact lenses

As the condition progresses, spectacles may fail to provide the patient with a satisfactory degree of visual acuity. Contact lenses improve vision by means of tear fluid filling the gap between the irregular corneal surface and the smooth regular inner surface of the lens, thereby creating the effect of a smoother cornea. Traditionally, lenses for keratoconus

have been the “hard” or rigid gas-permeable contact lens variety. For most patients with keratoconus, a three point touch contact lenses design is ideal (figure 1), and is preferred over apical clearance and apical touch designs. The base curve should be steep enough to provide a slight central touch, shown by thinning of fluorescein, at the corneal apex and slight touch mid-peripherally at 3 and 9 o’clock along the horizontal meridian. This creates three points of lens touch along the horizontal meridian. In mild to moderate keratoconus, the lens diameter selected is usually 7.5-8.5mm. A small size facilitates tear exchange and allows a steeper fit to accommodate the cone. Central nipple cones do best with small diameter lenses. When the cone is displaced peripherally, as with oval and globus cones, one usually ends up fitting a larger, flatter lens. Several specially designed contact lenses have been developed to facilitate fitting in advanced, difficult to fit keratoconus cases. **Soper** lenses are one of the best known lenses. This is a bicurve design with a steep central curve to accommodate the cone and peripheral curve to align with the peripheral cornea.



figure 1 fluorescein staining pattern from google.com

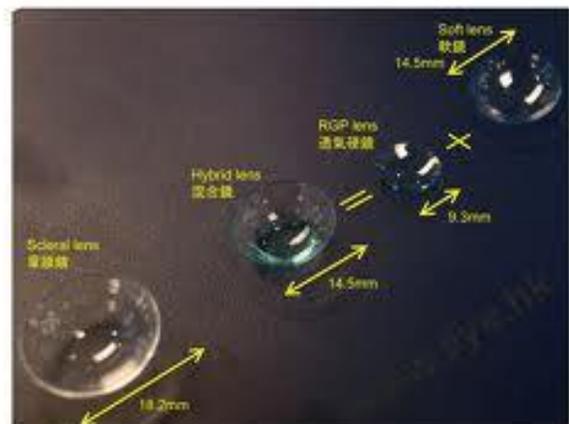


figure 2 contact lenses

Image 1 Source
http://www.clspectrum.com/content/archive/2011/May/images/CLS_May_A20_fig3.jpg

Image Source 2
http://en.wikipedia.org/wiki/File:Keratoconus_contact_lens_size.jpg

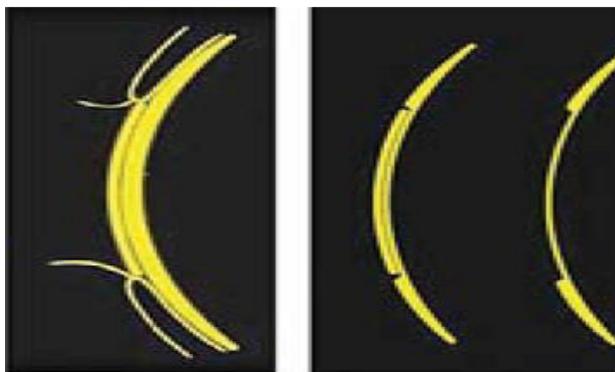


figure 3 traditional and custom piggyback lens

Image Source

<http://pacificu.edu/optometry/ce/courses/15167/images/Slide54.jpg>

<http://pacificu.edu/optometry/ce/courses/15167/images/Slide55.jpg>

They are fitted by varying the sagittal depth which in turn is done by varying the diameter of the lenses. **Mcguire** lenses are modified Soper lenses. They have central vaulting to minimise central bearing and peripheral cornea bears the major pressure. **Nicone** and **Rose-K** (figure2) designs have also been developed. The Rose K lens design is a fully flexible lens that works well on early to advanced keratoconus patients. Complex lens geometry, combined with the enhanced material benefits of Boston ES™, makes the Rose K lens the good fit enhancing patient comfort and visual acuity. Multiple parameters make fitting the Rose K lens possible for most keratoconic eyes. **Hybrid** lenses have been developed which are hard in the centre and encompassed by a soft skirt. Soft or hybrid lenses do not however prove effective for every patient. Some patients also find good

vision correction and comfort with a “piggyback” lens combination (figure 3), in which gas permeable rigid lenses are worn over soft lenses, both providing a degree of vision correction **Wave Custom Designed Contact Lens** is topography based designed contact lens. The corneal map is loaded into a lens designing software. This software is then used to design a lens specifically for that cornea.

Boston Scleral lenses Prosthetic device (BSLPD)

It is a fluid-ventilated gas-permeable contact lens that rests entirely on the sclera creating a fluid-filled space over the diseased cornea. They are sometimes prescribed for cases of advanced or very irregular keratoconus; these lenses cover a greater proportion of the surface of the eye and hence can offer improved stability and comfort. BSLPD has been worn with all day wearing comfort in many RGP lens intolerant patients⁵. High cost prohibits widespread usage.

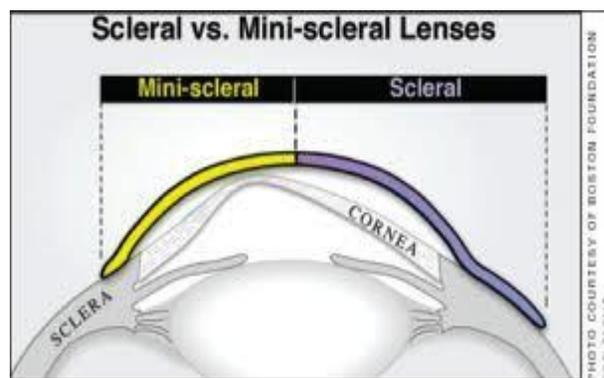


Image Source

http://allaboutdryeye.com/wpcontent/uploads/2011/11/scleral_lenses.png

The Boston Mini Scleral lens device (rests on peripheral cornea) has been recently developed for keratoconus patients.

Refractive surgery

Laser in situ keratomileusis (LASIK) or photorefractive keratectomy (PRK) is contraindicated in these patients because of a greater risk for scarring and excessive thinning leading to possible post-LASIK ectasia. Thorough topographic evaluation should be done to rule out keratoconus fruste or suspect before considering these procedures. For similar reasons, radial keratotomy has also generally not been used for keratoconic patient, unlike refractive procedures; phototherapeutic keratectomy (PTK) has been helpful for some selected keratoconus patients to reduce steepness of the cone and for nodular subepithelial scars in patients who have become contact lens intolerant. The resultant flattening of the cone makes contact lens fitting easier. The key to the safety of the procedure is that the very shallow ablation is not intended to have a refractive effect⁶.

Corneal Collagen Cross Linking With Riboflavin (C3-R)

Corneal collagen crosslinking with riboflavin (C3-R) is the name given to the treatment that combines the use of riboflavin (vitamin B2) with ultraviolet light for the treatment of keratoconus.

The riboflavin 0.1% eyedrops in 20% dextran are activated by approximately 30 minutes illumination with UV-A (370nm) light.



Figure 4 C3R procedure

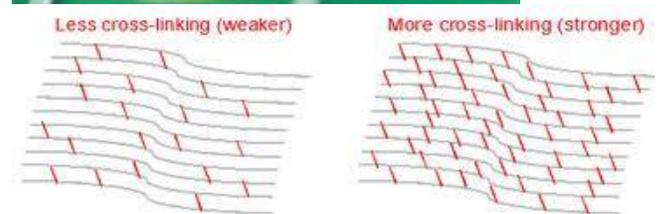


figure 5 increased crosslinking by C3R

Fig 5 Source

<http://www.optyco.co.uk/wpcontent/uploads/2012/07/crosslinking.png>

This treatment is applied to deepithelised cornea. The currently used UVA radiant exposure of 5.4 mJ/cm² and the corresponding irradiance of 3 mW/cm² are below the known damage thresholds of UVA for the corneal endothelium, lens, and retina (figure 4)^{7 8}. Recently The KXL™ System for Accelerated Cross-linking achieves speed by increasing the UVA power and reducing the exposure time (30mW/cm² for 3 minutes), thereby maintaining the same energy on the eye as standard cross-linking while reducing crosslinking time by an order of magnitude. C3-R augments the collagen cross-links within the stroma (figure 5) and so recovers some of the cornea's

mechanical strength⁸. The treatment has been shown to slow or arrest the progression of keratoconus, and in some cases even reverses it^{10,11,12} particularly when applied in combination with intracorneal ring segments^{9, 10}. In these cases, C3-R treatments stabilize keratoconus from getting worse as well as help the Intacs reverse the keratoconus steepening that had already occurred up to the time of the treatment. The need for penetrating keratoplasty might then be significantly reduced in keratoconus. Average flattening in central 'K' value reported in literature following C3R is 1.5 – 2 D which is responsible for improved contact lens fitting in many patients in whom it was not possible preoperatively.

Intrastromal Corneal Ring Segments

A recent surgical alternative to corneal transplant is the insertion of intrastromal corneal ring segments (figure 6). These inserts are designed to be placed at a depth of approximately two-thirds the corneal thickness and are surgically inserted through a small radial incision into a track created within the corneal stroma. The use of a femtosecond laser for Intacs channel creation seems as effective as mechanical dissection^{12, 13}. They are oriented horizontally in the cornea at 12 and 6 o'clock (figure 7). They shorten the corneal arc length and have a net effect of flattening the central cornea. The amount of flattening is determined by the insert's thickness. Rings are available in thicknesses of 0.250, 0.275, 0.300, 0.325 and 0.350

mm (recently 0.400 and 0.450 are also available).



fig.6 intacs ring

Fig

6 Source

http://www.harvardeye.com/procedures/images/intacs_orange_county.png

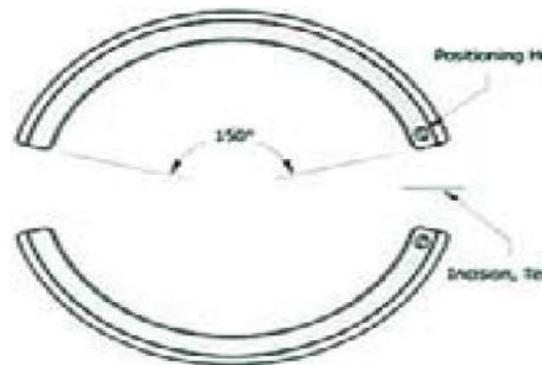


figure 7 placement of intacs ring

Source <http://www.fda.gov/ucm/groups/fdagovpublic/documents/image/ucm080963.gif>

Intacs are indicated for contact lens intolerant patients with early keratoconus who have minimal central stromal scarring. The two principal types of intrastromal rings available Intacs and Ferrara rings. Intacs are flatter and less centrally placed than the Ferrara rings. Intacs implantation is being increasingly considered and shown effective in early keratoconus case. Potential complications of intrastromal rings include accidental penetration through to the anterior chamber when forming the channel, post-operative infection of the cornea, and migration or extrusion of the segments. The rings offer a good chance of vision improvement even in otherwise hard to manage eyes and can always be a good option before taking up the patient for surgery^{14,15}. Contact lenses may be needed for keratoconus patients who have INTACS inserts and have a role in augmenting their vision. Contact lens tolerance was restored in over 80% of cases in a study. Rigid gas-permeable or toric soft lenses can be used.

Corneal Transplant

Penetrating keratoplasty (PK) has been the gold standard surgery for keratoconus patients with success rates of more than 90%¹⁷. Approximately 10% to 25% of cases of keratoconus will progress to a point where vision correction is no longer possible, thinning of the cornea becomes excessive, or scarring as a result of contact lens wear causes problems of its own, and a

corneal transplantation becomes required^{1,2}. In this procedure, the keratoconic cornea is prepared by removing the central area of the cornea, and a full-thickness corneal button is sutured in its place. Usually trephines between 8.0-8.5 mm are used. Fleischer's ring can be used as the limit of the conical cornea. Depending on the criteria used to assess the success rate, this surgery is 90% to 95% successful (figure 8). Most of these patients who are grafted for keratoconus are younger than the majority who are grafted for other reasons. Contact lenses are often required after this procedure for best visual rehabilitation. Recently the Femtosecond Laser was approved for performing Corneal Transplants (also known as I.E.K or Intralase Enabled Keratoplasty). An alternative is lamellar keratoplasty, a partial corneal transplant. The cornea is removed to the depth of posterior stroma, and the donor button is sutured in place. This technique is technically difficult, and visual acuity is inferior to that obtained after penetrating keratoplasty.



figure 8 Pre and post -PK- clinical photograph of a keratoconus patient

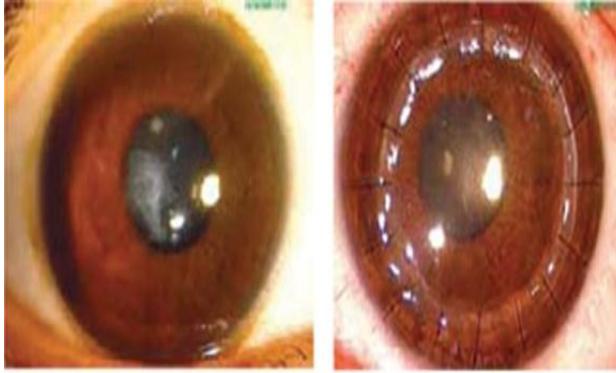


Figure 9: Pre and post-DALK clinical photograph of a keratoconus patient

Lamellar keratoplasty has recently been almost replaced by an alternative highly rewarding procedure of deep anterior lamellar keratoplasty (DALK)^{18, 19, 20}. In DALK, the patient's corneal endothelium is retained, giving some additional structural integrity to the post-graft cornea. The chance of a rejection episode is greatly reduced. DALK thus provides lower postoperative complications, faster postoperative recovery, fewer graft rejections and similar visual outcomes compared to PK (figure9). It is however a technically demanding procedure. A rarely performed but once tried procedure, thermokeratoplasty involved placing a hot ring (Holmium yag laser, 2100nm) along the base of the cone to heat and traumatize the cornea²¹, resulting in a corneal scar which reduces the corneal curvature, and allows a flatter contact lens to be fitted. The disadvantages of the procedure were a transitory corneal haze, development of corneal scarring and the fact that it does not preclude future keratoplasty. Epikeratoplasty is primarily suited for contact-lens-intolerant patients in whom scarring has not yet occurred²². In this procedure, the

central host epithelium is debrided, and the donor cornea is sewn over the keratoconic cornea. This is a rarely performed procedure today as the outcome is generally less favourable.

Phakic intraocular lens implantation

It can be used to correct high myopia and associated astigmatism of selected keratoconus patients. Anterior chamber phakic intraocular lens have also been combined with intacs with good results²³. The Intacs implantation is followed by toric phakic intraocular lens implantation to correct the residual myopic and astigmatic refractive error²⁴. Patients who are extremely nearsighted more than -10D might benefit from phakic intraocular lenses. Currently there are two type of these lenses approved by the FDA –the Verisys and the Visian ICL. These are implantable contact lens has been approved by the FDA for up to -20Diopters.

Keratophakia

Is an operation in which a partial-thickness corneal tissue graft is inserted into the cornea . The graft or 'lenticule' helps to restore the cornea to a normal thickness, and may also cause a change in the corneal surface profile, and so alter the cornea's refractive power. Keratophakia was originally conceived over fifty years ago by Dr José Barraquer as a treatment for the correction of hypermetropia (long-sightedness). It has also been used as a

treatment for myopia, and more recently for the management of keratoconus and corneal ectasia. In these latter conditions, the lenticule may be designed primarily to restore the corneal thickness to normal, rather than to change the corneal surface profile.

Thus to conclude, a number of treatments have been tried in keratoconus. Newer modalities like INTACS and C3R are helping to achieve visual rehabilitation and delaying the need for penetrating keratoplasty. RGP contact lenses are the mainstay in the rehabilitation of keratoconus patients. This holds true even though the patient may have undergone other procedures like keratoplasty, INTACS and C3R.

Recently a new microwave procedure, Keraflex KXL™, holds the promise of treating keratoconus while also correcting the associated refractive error²⁵. The procedure is carried out in two steps. In the first step, microwave energy is applied to a ring-shaped area of the cornea using an annular electrode. The energy penetrates the superficial stroma, inducing localized shrinkage of the collagen fibers. Step two entails a riboflavin-UV cross-linking procedure specifically within the microwaved area. The center and periphery of the cornea are masked using UV-blocking corneal shields. Riboflavin 0.1% is applied to the annulus following removal of the epithelium, and UV irradiation is carried out for 30 minutes. "UV cross-linking is used to improve the stability and extend

the lifetime of the flattening that Keraflex induces. The two procedures work synergistically.

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